

Abstract

Compounds, compositions and methods for promoting or inhibiting angiogenesis, and screening methods for identifying compounds are disclosed. The compounds bind to F1 ATP synthase, particularly to the alpha and/or beta subunits of F1 ATP synthase. When bound to these subunits, they can function as angiostatin agonists, antagonists, partial agonists, inverse agonists, or allosteric modulators. When the compounds mimic or enhance the activity of angiostatin, they inhibit angiogenesis. When the compounds inhibit the ability of angiostatin to bind F1 ATP synthase and are either inactive at inhibiting angiogenesis or directly promote angiogenesis, or if they inhibit the activity of angiostatin, they promote angiogenesis. The compounds can be, for example, antibodies, antibody fragments, enzymes, peptides, nucleic acids such as oligonucleotides, or small molecules. The antibodies can be monoclonal, humanized, or polyclonal antibodies. The compounds can be conjugated to or combined with various cytotoxic agents and/or labeled compounds. Methods for promoting angiogenesis can be used to introduce vasculature to areas in a patient that can benefit from such increased vasculature. Methods for inhibiting angiogenesis can be used to treat disorders mediated by angiogenesis, for example, tumors, autoimmune disorders such as rheumatoid arthritis, and the like.